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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/517,491	03/02/2000	Vivian Berlin	APBI-P06-036	4943

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 03/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/517,491	BERLIN, VIVIAN	
	Examiner	Art Unit	
	Robert A. Zeman	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *51-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *51-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed on 1-12-2004 is acknowledged. Claims 51-62 are pending and currently under examination.

Upon review of the record the finality of the previous Office action is withdrawn.

Priority

Applicant's arguments with regard to the claimed priority with regard to U.S. Application No. 08/360/144 has been fully considered and deemed persuasive. Consequently, the effective filing date of the instant application is December 20, 1994.

Terminal Disclaimer

The terminal disclaimer filed on 1-12-2004 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of any patent granted on Application number 6,464,974 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections Withdrawn

The rejection of claims 51-62 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2, 6-7, 9, 11, 13 and 16-17 of U.S. Patent No. 6,464,974 is withdrawn in light of the Terminal Disclaimer filed on 1-12-2004.

The rejection of claims 51-62 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Berlin et al. (WO 95/33052) is withdrawn since the cited reference is no longer available as prior art under 35 U.S.C. 102(b).

New Grounds of Rejection

USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 51-62 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a vast genus of antibodies, which bind to a mammalian RAPT1 protein (optionally with a sequence identity of at least 90 percent to SEQ ID NO:12).. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession of the

claimed invention. To adequately describe the genus of antibodies, Applicant must adequately describe the peptides encompassed by claim 1 to which the antibodies bind.

However, the specification does not disclose distinguishing and identifying features of a representative number of members of the genus of peptides to which the claims are drawn, such as a correlation between the structure of the peptide and its recited function, so that the skilled artisan could immediately envision, or recognize at least a substantial number of members of the claimed genus of antibodies. Moreover, the specification fails to disclose which amino acid residues are essential to the function of the peptide, or which amino acids might be replaced or deleted so that the resultant peptide retains the activity of its parent, or by which other amino acids the essential amino acids might be replaced so that the resultant peptide retains the activity of its parent. Therefore, the specification fails to adequately describe at least a substantial number of members of the genus of peptides to which the claims refer; and accordingly the specification fails to adequately describe at least a substantial number of members of the claimed genus of antibodies.

MPEP § 2163.02 states, "[a]n objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed' ". The courts have decided:

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

See *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable

from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.,* 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, ``Written Description'' Requirement (66 FR 1099-1111, January 5, 2001) state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Moreover, because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant were in possession of the claimed invention at the time the application was filed.

The *Guidelines* further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing

only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. As evidenced by the teachings of Skolnick et al., the art is unpredictable. Skolnick et al. (*Trends in Biotechnology* **18**: 34-39, 2000) discloses the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (see, e.g., the abstract; and page 34, *Sequence-based approaches to function prediction*). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see, in particular, the abstract and Box 2). Thus, one skilled in the art would not accept the assertion, which is based only upon an observed similarity in amino acid sequence, that a variant of the polypeptide of SEQ ID NO:12 is a mammalian RAPT1 protein. Therefore, because the art is unpredictable, in accordance with the *Guidelines*, the description of claimed antibodies is not deemed representative of the genus of peptides to which the claims refer.

Finally it should be noted that the courts have recently decided in Randolph J. Noelle v Seth Lederman, Leonard Chess and Michael J. Yellin (CAFC, 02-1187, 1/20/2004) that

a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See Enzo Biochem II, 323 F.3d at 965; Regents, 119 F.3d at 1568. Therefore, based on our past precedent, as long as an applicant has disclosed a "fully characterized antigen," either by its structure, formula, chemical name, or physical properties, or by depositing the protein in a public depository, the applicant can then claim an antibody by its binding affinity to that described antigen.

Noelle did not provide sufficient support for the claims to the human CD40CR antibody in his '480 application because Noelle failed to disclose the structural elements of human CD40CR antibody or antigen in his earlier '799 application. Noelle argues

that because antibodies are defined by their binding affinity to antigens, not their physical structure, he sufficiently described human CD40CR antibody by stating that it binds to human CD40CR antigen. Noelle cites Enzo Biochem II for this proposition. This argument fails, however, because Noelle did not sufficiently describe the human CD40CR antigen at the time of the filing of the '799 patent application. In fact, Noelle only described the mouse antigen when he claimed the mouse, human, and genus forms of CD40CR antibodies by citing to the ATCC number of the hybridoma secreting the mouse CD40CR antibody. If Noelle had sufficiently described the human form of CD40CR antigen, he could have claimed its antibody by simply stating its binding affinity for the "fully characterized" antigen. Noelle did not describe human CD40CR antigen. Therefore, Noelle attempted to define an unknown by its binding affinity to another unknown. As a result, Noelle's claims to human forms of CD40CR antibody found in his '480 application cannot gain the benefit of the earlier filing date of his '799 patent application.

Moreover, Noelle cannot claim the genus form of CD40CR antibody by simply describing mouse CD40CR antigen.

Consequently, since Applicant has not fully characterized the antigen to which the claimed antibodies bind, the written description requirements under 35 U.S.C 112, first paragraph have not been met.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 51-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sabatini et al. (Cell Vol. 78, pages 35-43, July 15, 1994) in view of Campbell (Monoclonal Antibody Technology, Elsevier, N.Y. 1984; chapter 1, pages 1-32).

Sabatini et al. disclose the amino acid sequence for mammalian RAFT1 that fully incorporates SEQ ID NO :12 of the instant application (see Figure 5 and STIC search printout, attached). Sabatini et al differ from the instant invention in that they do not disclose antibody preparations (either monoclonal or polyclonal) that are specifically immunoreactive with a mammalian RAPT1 protein and do not substantially cross react (binding affinity of less than 10 percent) with a fungal TOR1 or TOR2 protein or antibodies that are specifically immunoreactive with a RAPT1 protein having an amino acid sequence that is at least 90 percent identical to SEQ ID NO:12 of the instant application. Campbell discloses that "It is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)"[see page 29]. Consequently, it would have been obvious to one of skill in the art to make antibodies to the proteins disclosed by Sabatini et al. Moreover, since SEQ ID NO:12 codes for the biologically active region of the RAFT1 protein disclosed by Sabatini et al., any antibodies raised against said RAFT1 protein would bind (i.e. immunoreact) with a protein with a 90 percent identity to SEQ ID NO:12.

Claims 51-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (Nature Vol. 369, pages 756-758, June 30, 1994) in view of Campbell (Monoclonal Antibody Technology, Elsevier, N.Y. 1984; chapter 1, pages 1-32).

Brown et al. disclose the amino acid sequence for human FRAP which fully incorporates SEQ ID NO :12 of the instant application (see page 757 and STIC search printout, attached). Brown et al. differs from the instant invention in that they do not disclose antibody preparations (either monoclonal or polyclonal) that are specifically immunoreactive with a human FRAP protein and do not substantially cross react (binding affinity of less than 10 percent) with a fungal TOR1 or TOR2 protein or antibodies that are specifically immunoreactive with a RAPT1 protein having an amino acid sequence that is at least 90 percent identical to SEQ ID NO:12 of the instant application. Campbell discloses that "It is customary now for any group working on a macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)"[see page 29]. Consequently, it would have been obvious to one of skill in the art to make antibodies to the proteins disclosed by Brown et al. Moreover, since SEQ ID NO:12 codes for the biologically active region of the RAFT1 protein disclosed by Brown et al., any antibodies raised against said RAFT1 protein would bind (i.e. immunoreact) with a protein with a 90 percent identity to SEQ ID NO:12.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (571) 272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on (571) 272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Robert A. Zeman
March 4, 2004

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